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PLACENTAL DEVELOPMENT.

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ENTWICKELUNG DER PLACENTA.

BY HENRY O. MARCY, M.D.,

Of Boston, Mass.

Four years ago, Italy mourned the loss of one of her most brilliant sons, Count Ereolani, of Bologna, a man, like Germany's great scientist, Virchow, alike celebrated as a leader in the great political struggles for the elevation of his people and an enthusiastic devotee of science. Educated in the school of the great Antonio Alessandrini, whose learned diligence he early imitated, in the most lamentable poverty of means, he contributed to the foundation of those monuments of marvelous industry, the museums of Comparative Anatomy and Veterinary Pathological Anatomy, of Bologna. The high renown which he had acquired in the sciences and his profound learning procured him many honors. He attained the highest offices of Bologna's most famous university, being several times President of the Medical Faculty and twice Rector of the University. Aided by the government, he was enabled to erect new buildings and furnish the School of Veterinary Medicine with modern appliances for successfully carrying on original investigations in the department of comparative anatomy and physiology. Although widely known by his many original contributions to science, he is especially deserving of and receives world-wide repute for his long-continued investigations of the placental development in vertebrates.

More than ten years since, there first came to my notice an unpretending volume, published in Africa, a translation in French, by Dr. Andreini, of a certain portion of Professor Ereolani's investigations, which as a prize essay had received an award from the Academy of Sciences at Paris. In our Harvard Library, I found in the *Transactions* of the Academy of Sciences at Bologna the original papers with illustrations, published from time to time, having been presented by him as contributions to the Academy. Convinced of the singular value, as well as the originality of his work, I collated and presented to the English reading public the first edition, which included all his anatomical researches, up to the date of the publication, the last chapters of which were written specially for this English edition. In 1880 was published a second and enlarged edition, which included also Professor Ereolani's researches upon the pathological conditions of placental development, with a careful analytical review of the whole subject, written while yet suffering from the dire malady which speedily thereafter terminated his life. During all this period, I myself have carefully studied the changes incident to the uterus in the reproductive state in woman, and, as far as opportunity has been afforded me, comparative studies in animals. I am thereby convinced more than ever of the correctness of Professor Ereolani's teaching, and hold in admiration the remarkable ability and skill by which he arrived at conclusions so far-reaching, and demonstrated with singular clearness nature's uniform law of the unity of anatomical type in a simple and fundamental plan of embryonic nutrition and development.

The present occasion offers opportunity only to review very briefly some of the more important deductions to be made therefrom. In our own profession the study of reproduction has been chiefly limited to the human species, and nothing is more complex or confusing, veritably a labyrinthian riddle, than the fully developed human placenta. The uterine mucosa had been studied with some care by many investigators, in both woman and in the lower animals, for generations. To Malpighi, of the fifteenth century,

we date the first reliable demonstrations upon the mucous membrane in woman and in some species of the lower animals. He described the openings of the utricular glands into the uterine cavity, and observed that these glands, at least in the cow, increased in size during pregnancy. When we consider the lack of optical instruments in his day, his observations are worthy of special comment. Little was added to this anatomical knowledge by scientists until within the present generation.

Professor Ereolani, as the trained comparative anatomist, early devoted his attention to a careful microscopic differentiation of the mucous membrane with its glandular structure, in all the various species which he was enabled to bring under his observation. This naturally led to the investigation of the more complicated question of their function during pregnancy, and thus, little by little, was brought into differential study placentation.

The placenta is ordinarily subdivided into diffused, multiple and single. Perhaps the simplest form of the first is found in the mare. Over the whole maternal portion of the uterus, in this animal, there are developed a series of secreting glands of follicular character, and into these it is easy to trace the villi of the foetal portion of the placenta. A foetal villus is little more than a vascular loop covered with epithelium. The glandular follicle is equally simple in anatomical construction, and also lined with epithelium; the one, a villus of secretion, the other of absorption. This is the simplest possible type of the double structure of the placenta.

The multiple placenta of the cow offers the simplest form of this kind of placenta, common to ruminants. The glandular maternal organ is here modified, although it does not lose its elementary form of a simple follicle. The modification consists chiefly in the uterine follicles being placed parallel to the surface, and sometimes superimposed upon each other, instead of, as in the diffused placenta, being disseminated vertically over the whole internal surface of the uterus.

In the dog and cat the follicles are extraordinarily elongated into tubular glands, as it were, which are closely packed against the foetal villi.

In woman, all that relates to the form itself of a glandular follicle, is completely lost, but the fundamental parts of a secreting organ, that is to say, the walls and cells, in a word, the gland and its secretion, are persistent.

The lesson taught by comparative anatomy lies in the following of these changes in the more simple form of placentation, and observing that in each the nutrition of the foetus is provided for upon this simple plan. Having once determined with accuracy these facts, we are then, for the first time, prepared to devote ourselves intelligently to the discussion of the placental development in woman. It is sufficient here to make the simple statement of that which may be conceded as an accepted fact, that in woman the mucous membrane is reduced to a simple layer of epithelial cells, and that in impregnation there is a proliferation and destruction of these cells over the entire surface of the uterus. This destructive process of the epithelium on the internal surface of the uterus is, in all cases, indispensable, because this is what facilitates the setting up of the neo-formative changes from which will result the maternal portion of the placenta. This denudation of the internal surface of the uterus teaches that the formation of the decidua and the placenta is due, neither to a tumefaction nor to a transformation of the anatomical elements preëxistent at the time of conception in the uterine mucous membrane.

The neo-formative process of the maternal portion of the placenta consists in the production of new vessels which are distinguished from the ordinary uterine vessels; first, the arterial as well as the venous vessels, have only a simple endothelial wall; second, on the external surface of their wall is elaborated a layer, more or less thick, of special cells, not separable from the wall of the vessel. These are the so-called decidual or placental cells.

That the foetal portion of the placenta is itself due to a neo-formative process has not been and cannot be questioned. It is from the constant relation established between these two parts of neo-formation that the placenta is developed. The manner in which this relation is established, gives rise to the different forms of placenta known in the mammalia. Except as viewed by Ercolani, the opinions which have been entertained, concerning the origin of the cells which enter so largely into the formation of the maternal part of the placenta, have been exceedingly vague and uncertain. Professor Turner, although concisely affirming, with Owen, that without decidua there is no formation of placenta, does not touch the important question of the origin of the decidua.

Professor Kölliker confines himself to the remark that the decidua is a transformation of the uterine mucous membrane, and not a new membrane, or the product of an exudation, as was once believed. It may be observed, however, that Professor Kölliker does not attempt to show which are the elements in the mucous membrane that compose the decidua, nor by what means they are transformed, although such an investigation should be of the highest interest to him, since the glandular follicles of new formation, as demonstrated by Prof. Ercolani, and largely confirmed by Turner, were only declared by him to be tumefactions of the preëxisting uterine mucous membrane, formed during pregnancy and disappearing after delivery.

The elementary and typical form of the two parts constituting the placenta in the mammifera, is not imaginary, but is demonstrated in its simplicity, by careful observation. It is easily recognized in the foetal portion in the villi of the chorion, in the simpler forms of diffused placenta, and at the beginning of development in the human species. In the maternal portion, the simple elementary form is found to be developed, and maintained through the whole period of gestation, in the uterus of certain viviparous fishes. The manner in which the relation between the two parts is established may be by simple proximity, contact, or by intimate cohesion. When the relation is that of simple nearness, the maternal portion of the placenta manifestly presents the form of a glandular organ, and has its limitation by the repetition of secretory villi upon the inner surface of the uterus, which, uniting with each other in various ways, give rise to the formation of crypts, or glandular follicles, single or compound, into which enter the absorbent villi of the chorion.

When the relation is more intimate and an adherence takes place between the two parts before mentioned, as in the single placenta, the glandular character is concealed by the fact of the adhesion, but the fundamental condition remains constant. The contact in this case is direct, between the vessel of the absorbent villus and the epithelium of the secreting villus, which is never lost. Only two very simple changes occur in the fundamental parts of the placenta when single, and they are the factors of the manifold differences which are observed. First, the loss of the epithelium of the absorbent villus, which is not important, since there is established direct contact of the vessel of the foetal villus with the secretory epithelium of the maternal villus, and this fact is constant. Second, the dilatation, or ectasia of the vessel in the maternal villus, and this fact is remarkable only in the placenta of the quadrumana and in woman.

The ectasia in the maternal vessels, already shown under a rudimentary form in the placenta of certain mammals, had been indicated by Eschricht and Turner, as representing the large lacunae which are observed in the placenta of some of the quadrumana, and in that of the human species. But these supposed lacunae have been the chief, if not the only stumbling-block to the exact knowledge of the structure of the human placenta, although anatomists were aware that ectasia takes place in the placental vessels in their phases of development.

It is known that, in the earliest period of pregnancy, the placenta in the human

species is represented by a layer formed of a rather compact cellular mass called decidua serotina, or placental decidua, in the midst of which runs a network of capillary vessels. From the surface of the chorion which is in contact with this layer, the villi are formed, at first simple, which penetrate among the cells of the serotina. For a time the relation between these two parts of the placenta is not so close that they cannot be separated. It is known, moreover, that, with the progress of the development, the vessels of the primary capillary network become ectatic, and the primary simple chorionic villi proliferate and become arborescent. If we could loosen and skillfully separate without tearing, the compact mass formed by the cells of the decidua serotina, before the vessels become ectatic, we should obtain exactly what comparative anatomy has very clearly shown in the single placenta of certain mammals, the dog and cat, for example, namely, a large meshed network of placental vessels everywhere surrounded by a cellular layer, placental cells.

We may easily demonstrate, in the placenta of early abortions, the gradual development of the lacunæ by ectasia, from the beginning, in the network of the capillaries amidst the mass of the placental cells, while the villi of the chorion are still quite simple.

Robin described this condition with great accuracy. The formation of the lacunæ precedes, therefore, the formation of the tufts of the villi, and cannot be an effect, since they are observed before the existence of the cause assigned by Prof. Kölliker.

Still further and more conclusive evidence upon the formation of the lacunæ, independent of the presence of the foetal villi, may be found in the structure of the so-called uterine decidua in cases of extra-uterine pregnancy, and there is found the exact and isolated anatomical structure of the maternal portion of the placenta, in which exist lacunæ, through ectasia of the vessels, without any trace of the foetal villi. Kölliker himself teaches that the short utero-placental arteries, when they penetrate into the placenta, lose their distinctive anatomical characteristics, that is, they no longer have muscular fibres or elastic elements; and their whole wall is formed by an endothelial layer, covered with a thin sheath of connective tissue, which disappears and blends with the decidua serotina. He further states "that the veins are no longer to be distinguished from the arteries, and all traces of both are lost in the interior of the placenta where alone the large lacunæ are found."

In 1876, De Sinèty called attention to an important demonstration in its bearing upon the above view. He noticed that the cells of the decidua in woman form a circular sheath about the placental vessels. However, if the facts observed by him in the completely developed human placenta harmonize with those already noticed early in its development, when there is seen a minute network of capillaries that become ectatic in the midst of the cells of the decidua or placental serotina, we shall be convinced that it is not the walls of the utero-placental vessels which are lost in these cells, as was indicated by Kölliker, but that so enormous a dilatation has taken place as to render it difficult to perceive the endothelium and to separate it from the placental cells that are elaborated by their external walls.

The chorionic villi in woman, while yet existing in its proliferation around the entire sac, are always covered with an epithelium of their own. The chorionic villi, away from the placental site, in the atrophic state of advanced foetal development, may still be seen covered with epithelium, although shrunken and atrophied.

But in the intimate cohesion with the maternal villi in the developing placenta, the epithelium covering the chorionic villus is lost. This may be easily demonstrated by observations upon the placenta in abortions, where the death of the foetus has for some time preceded the separation of the placenta. Here the foetal villus is shriveled and shrunken, and is easily defined as distinct from the maternal villus with its layer of actively growing placental cells.

The belief that the lacunæ are really large cavities, as they seem to be microscopically, and not the maternal vessels greatly dilated, is still generally taught, and through this belief two other deceptive appearances are accepted as actual truths, namely, that the chorionic villi float in the maternal blood, and that the epithelium covering them appertains to the fœtus instead of to the mother. Setting aside these fundamental errors, many facts already observed by able anatomists in the human placenta which have remained doubtful or were wrongly interpreted, now receive, under the teaching of Ercolani, a clear and precise explanation.

The belief that the villi in the placenta of woman float in the blood of the lacunæ, generated the physiological error that the nutrition of the fœtus, not only in the human species, but in all mammals, took place through an osmotic exchange of the two bloods, although in the case of the diffused placenta the facts openly contradict such an assertion. Beside, in all cases where the placenta is single, the vessel of the absorbent villus (fœtal) never comes in contact either with the blood or with the wall of the maternal vessel. There is always interposed between the walls of the two vessels, and, consequently, of the two bloods, a cellular layer which is the epithelium of the maternal villus, and that this is secretory is confirmed by the obvious glandular appearance which is observed in many animals in the maternal portion of the placenta when it has the diffused form.

Briefly reviewed, these changes take place in woman during pregnancy. The uterine mucous membrane, which consists of a simple layer of the epithelium closely attached to the subjacent muscular wall, disappears. It is replaced by a layer of decidual cells, proliferated from the vascular network of the uterine wall. The uterine glands are not destroyed, but, on the contrary, are increased in size. The constant secretion therefrom forms openings through the decidua vera, which may easily be traced by the unaided vision, as a sieve-like perforation. By the proliferation of the serotinal cells at the placental site, these glands are, by the pressure from their own obstructed secretion, dilated and altered, and this forms the strata, called by Kölliker the non-deciduous portion of the placenta. Traces of these glands may be observed, even to the termination of pregnancy, but none whatever are found in the deciduous stratum of the placenta, as defined by Kölliker, where it would be expected that they would be found, if, as claimed by him, the placenta is a transformation of the uterine mucosa.

All anatomists agree that the stratum where the placenta is formed is developed from a mass of cellular or decidual elements, traversed by a vascular network, with endothelial walls only during the first months of pregnancy, and that among these elements the fœtal villi are buried. During the first three months of pregnancy, the fœtal villi can be separated from the maternal portion without a laceration of the latter, in the same way as in the mammiferous non-deciduates.

The second period of development, by the universal consent of anatomists, begins with the establishing of two facts, the rapid and exuberant proliferation of branches from the trunk of the fœtal villi, and the ectatic process in the network of the maternal vessels. These conditions taking place contemporaneously, in a limited and circumscribed space, it must necessarily follow, as the result of simple physical and mechanical law, that the branches of the proliferating villi should press against the endothelial walls of the vessels, which are, at the same time, thinned and dilated. The ultimate result is, that the walls of the vessels, at first bent in simply toward the internal cavity of the dilating vessel, must, as the process of aneurism becomes more and more pronounced, completely invest the villus, aided also by the tension exercised upon the walls of the vessel by the rapidly proliferating branches of the villi.

Weber and Virchow observed this condition in abortions, describing the tufts of the villi as making a complete hernia in the maternal vessel. Resulting therefrom the epithelial covering of the chorionic villus disappears. Intimate union with the intro-

flected wall of the maternal vessel, lined with its layer of decidal cells, ensues, and the picture of the villi swimming in the lacunæ is complete.

Professor Ercolani sums up his conclusions as follows: In all the vertebrates the nutritive material, which is to serve for the growth of the fœtus, is provided by the mother. In mammals it is supplied by the maternal portion of the placenta gradually, as the fœtus develops. In the oviparous vertebrates, the material, in the quantity necessary for the development of the fœtus, is emitted in a mass from the mother in the egg. In the mammiferous, as in the oviparous animals, the absorbent or fœtal part does not change, and it is by means of an absorbent villus, more or less complicated, that the material elaborated by the mother is conveyed to the fœtus. There is, therefore, but one law, a physiological modality, that governs the nutrition of the fœtus in vertebrates.

There is also always preserved an unfailing typical unity of anatomical structure in the placenta, in the different classes and species of mammals, and the variety and multiplicity of forms depend only on a few very simple modifications, observable in the two fundamental parts, the fœtal and the maternal, which constitute the placenta in the mammifera and in the human species.

DISCUSSION.

Prof. SIMPSON said the obstetricians were much indebted to Dr. Marey for coming from the Section over which he was presiding, * to give them such a lucid and instructive exposition of the recent observations on the structure and development of the placenta. He heartily endorsed Dr. Marey's admiration of the illustrious professor of Bologna, whom he (Prof. Simpson) had the satisfaction of seeing at work in his laboratory, in 1872, and whose researches he followed with greater confidence, from the impression he had then gained of Ercolani's earnestness and honesty of purpose. The method Dr. Marey has adopted of expounding his views as to the placental relations was a happy one, and, indeed, the only satisfactory one, proceeding from the simplest to the most complicated plans of placentation. The problem solved in the construction of the placenta, was how to bring fœtal and maternal blood vessels into such relations as would admit of interchange of effete and nutritive materials between the one system and the other. In the simplest forms, as in the ridged placenta of the sow, or the diffused placenta of the mare, the whole surface of the chorion was vascular and applied to a corresponding hyperæmic surface of the uterine mucosa, slight fœtal ridges, or projections, fitting into shallow furrows or depressions, with such slender connection that when the ovum was expelled, not even the epithelial surface of the uterus was affected. In the polyotyledonary placenta of the ruminants, specially enlarged groups of fœtal villi on limited portions of the chorionic surface dipped down into specially developed crypts in limited areas of the uterine mucosa, and when the ovum was expelled, the fœtal villi were often found to have carried off some of the uterine epithelium attached to their extremities. In the still more limited zonary placenta of the carnivora, the fusion became still more intimate, so that on expulsion of the ovum some of the sub-epithelial decidual tissue was carried off by the fœtal villi, without, however, causing any necessary injury to the maternal blood vessels. Where the placental site became still more distinctly limited, as in the case of the two-toed sloth, Sir William Turner, to whose researches Dr. Marey had referred, and whom he (Prof. Simpson) was proud to claim as his colleague and friend, had made the interesting observation that the capillaries in the maternal mucosa had become distended at parts presenting an aneurismal or

* Gynæcology.

varicose appearance. This helped to the understanding of the changes that took place in the capillaries of the human scrotina, which probably passed through a similar stage before becoming developed into the placental sinuses, which Weber had described as "colossal capillaries." In the human placenta, the fusion of chorionic and mucosal tissues had become so intimate and intricate, that when the ovum was thrown off, the chorion carried with it the greater part of the thickness of the uterine mucous membrane, leaving only a thin layer corresponding to the blind extremities of the follicles attached to the subjacent muscular wall. The exact condition of the capillary arrangement in the placenta, it was right to remember, could not yet be regarded as definitively settled. In a recent work published by the lamented Schroeder, in conjunction with some of his pupils, one of these had an article denying the existence of the cavernous spaces usually supposed to exist in the placenta, and further observations must be made at various stages of development before a true anatomy of the placental vessels can be arrived at. As regards the simple layer of epithelial cells, which most observers now recognize as the only intermediary between the maternal and foetal blood, he (Prof. Simpson) had, at one time, followed Virchow in regarding them as of foetal origin. The more recent observations, however, of Turner and others, had convinced him that Dr. Marey was correct in following Ercolani, who was the first definitely to declare them to be maternal in their origin.

